ORIGINAL RESEARCH

A Value-Based Analysis of Hemodynamic Support Strategies for High-Risk Heart Failure Patients Undergoing a Percutaneous Coronary Intervention

David Gregory, MPA; Dennis J. Scotti, PhD, MBA; Gregory de Lissovoy, PhD, MPH; Igor Palacios, MD; Simon Dixon, MD; Brijeshwar Maini, MD; William O'Neill, MD

Background: The economic burden of heart disease is heavy and growing. As advanced technologies for treating heart disease become available, decision makers need to be able to assess the relative value of such options against existing standards of care.

Objectives: To compare the clinical and economic benefits of a percutaneous ventricular assist device (pVAD) versus an intra-aortic balloon pump (IABP) observed during the 90-day duration of the PROTECT II clinical trial, and to supplement these findings with a simulation of the longer-term value of this technology through the use of a Markov model to estimate the incremental cost-effectiveness of a pVAD relative to an IABP, in terms of quality-adjusted life-years (QALYs).

Methods: Hospital bills were collected for patients enrolled in the PROTECT II trial who received hemodynamic support for high-risk percutaneous coronary intervention (PCI) provided by a pVAD (Impella 2.5) versus a conventional IABP during a 90-day episode of care (EOC). Length of stay, charges, and costs were analyzed for the index admissions, intensive care unit confinements, readmissions, and overall EOC. In addition, a probabilistic Markov model was used to project these parameters and their impact on a patient's quality of life for up to 10 years in relation to a pVAD versus an IABP.

Results: Hospital costs for the index admission were lower for the IABP compared with the pVAD ($33,684 vs $47,667; P <.001), whereas readmission length of stay and costs were lower for the pVAD versus the IABP (5 days vs 7 days; and $11,007 vs $21,834, respectively; P <.001). The total 90-day hospital charges were similar for the pVAD and the IABP ($172,564 vs $172,758, respectively; P = .785); however, the total 90-day EOC cost was lower for the IABP than for the pVAD ($44,032 vs $53,171, respectively; P <.001). The median hospital days for the entire EOC were 7 days for the pVAD versus 9 days for the IABP (P = .008). Critical care stays were considerably shorter for a pVAD than for an IABP on readmissions (3.88 days vs 7.00 days; P = .145). Reduction in major adverse cardiovascular and cerebrovascular events resulted in a projected gain of 0.26 QALYs over 10 years, yielding an incremental cost-effectiveness ratio of $39,389/QALY.

Conclusions: For high-risk patients with advanced heart failure undergoing PCI, the new pVAD reduced major adverse events, critical care and readmission length of stay, and readmission cost over the 90-day EOC, and was determined to be cost-effective over the long-term. These findings can assist decision makers in forming value-based judgments with regard to new hemodynamic support strategies.

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Disclosures are at end of text

Mr Gregory is Executive Vice President and Partner, Presscott Associates, a Division of ParenteBeard, LLC, New York, NY; Dr Scotti is the Alfred E. Driscoll Professor of Healthcare & Life Sciences Management, Fairleigh Dickinson University, Teaneck, NJ; Dr de Lissovoy is Adjunct Associate Professor, Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; Dr Palacios is Director, Cardiac Catheterization Lab, Massachusetts General Hospital, Boston, MA; Dr Dixon is Chair, Cardiovascular Medicine, Beaumont Health System, Royal Oak, MI; Dr Maini is Director, Advanced Cardiac & Endovascular Interventional Laboratory, Cardiovascular Research & Education, PinnacleHealth, Wormleysburg, PA; Dr O'Neill is Medical Director, Center for Structural Heart Disease, Henry Ford Hospital, Detroit, MI.

More than 1 in 3 American adults have at least one type of cardiovascular disease, which is the leading cause of death in the United States for men and women.[1] The total annual burden of heart disease is estimated to be $312.6 billion in combined direct and indirect costs.[1] In addition to an overall annual cost of more than $34 billion,[2] heart failure is one of the main medical conditions necessitating acute hemodynamic support. Advanced heart failure is the leading source for hospital readmissions among the Medicare population and commercial populations.[3-8] Symptomatic patients with multivessel coronary artery disease or unprotected left main and depressed left ventricular functions carry a high risk for morbidity and mortality while undergoing percutaneous coronary intervention (PCI), which is a common treatment for such patients.

Patients with heart failure typically have extended nonviable myocardium and a cardiac reserve that is too low to respond to temporary ischemia during percutaneous procedures. This often leads to hemodynamic instability, from severe hypotension to cardiogenic shock or even death. Temporary hemodynamic support is often used during these high-risk procedures to prevent catastrophic hemodynamic decompensation and to improve heart function and outcomes. Such an approach is frequently the only option for select patients who have been turned down for cardiac surgery because of their high clinical and coronary anatomy risks.

The traditional treatment for patients with high-risk PCI has been the intra-aortic balloon pump (IABP), although its effectiveness has been questioned[9-13] and has led patients and providers to express the need for alternative therapeutic options. The newly introduced percutaneous ventricular assist device (pVAD), Impella 2.5, is unique among the few currently available pVADs by virtue of its miniaturized size, self-contained motor, and because its placement does not require invasion of the heart muscle.

The Impella 2.5 is a minimally invasive percutaneous catheter-based device that is powered and controlled by its console and is designed to provide partial circulatory support. The Impella pump pulls 2.5 L/min of blood from the left ventricle through an inlet area near the tip and expels blood from the catheter into the ascending aorta (**Figure 1**). The 9F catheter/12F motor pump can be inserted via a standard catheterization procedure through the femoral artery, into the ascending aorta, across the valve, and into the left ventricle.

By contrast, the IABP, which has been in use since the late 1960s, is a volume displacement catheter that relies on the native heart function to provide continued systemic forward flow, requiring varying doses of inotropic agents to improve contractility.

KEY POINTS

- Heart failure is the main cause for hospital readmissions in patients with heart disease.
- Heart failure is a leading condition requiring acute hemodynamic support, especially in patients undergoing high-risk percutaneous coronary intervention.
- This is the first economic analysis to compare the resource utilization and costs for an intra-aortic balloon pump (IABP)—the current standard of care for this patient population—and a newly introduced percutaneous ventricular assist device (pVAD) in patients requiring acute hemodynamic support.
- The results show that index hospitalization costs were lower for the IABP versus the pVAD ($33,684 vs $47,667), but readmission length of stay and costs were reversed; both were lower in the pVAD cohort than in the IABP cohort (5 days vs 7 days; and $11,007 vs $21,834).
- The major adverse event rate was 22% lower and the major adverse cardiovascular/cerebrovascular event rate was 29% lower in the pVAD cohort versus the IABP cohort.
- The long-term analysis further shows the potential value of pVAD use versus IABP in terms of quality-adjusted life-years and cost-effectiveness.

A key difference between this new pVAD and the IABP is the pVAD's ability to directly unload the left ventricle, thereby augmenting coronary flow and providing better hemodynamic support compared with the traditional IABP.[14-16] No studies have been published that compare the resource utilization and the treatment costs associated with the pVAD versus IABP from a US perspective.

The PROTECT II study was a multicenter, randomized trial designed to assess whether a high-risk percutaneous revascularization strategy with the support of the new pVAD technique would result in better outcomes compared with a revascularization strategy with the support of an IABP.[14] Using the clinical and economic data from this clinical study, we present the first resource utilization and relative value assessment of pVAD in relation to the current standard of care, namely, the IABP. The purpose of this present study is to (1) evaluate and document the clinical and economic benefits of this pVAD during the 90-day duration of the PROTECT II trial, and (2) to supplement these findings with a simulation analysis of the longer-term value of this technology through the use of a Markov model to estimate the incremental cost-effectiveness of a pVAD versus an IABP expressed in terms of quality-adjusted life-years (QALYs).

Figure 1 The Impella 2.5 Percutaneous Catheter-Based Device

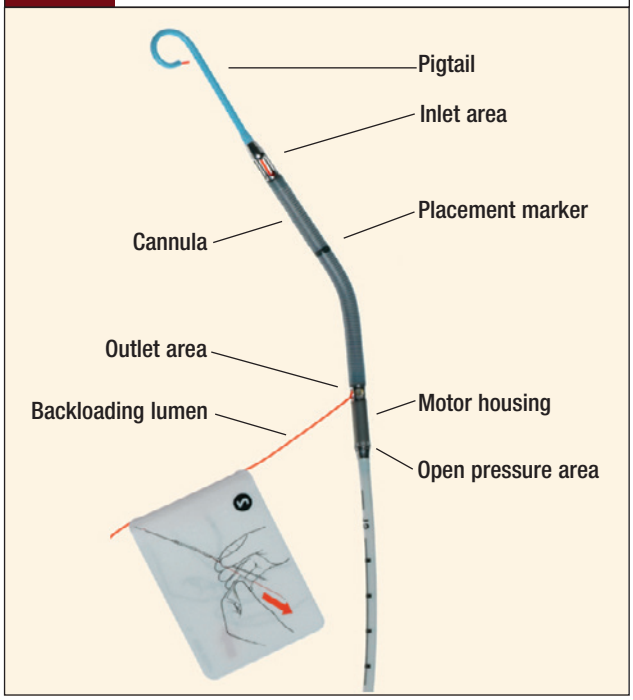


Table 1 Baseline Characteristics of the Study Population

Characteristics	IABP (N = 211)	pVAD (N = 216)	*P* value
Age (± SD), years	67 (± 11)	68 (± 11)	.583
Male sex, %	82.0	80.6	.704
Current NYHA class III/IV, %	54.9	58.9	.434
Left ventricular ejection fraction, %	24.0 (± 6.3)	23.3 (± 6.3)	.258
Nonsurgical candidate, %	64.5	63.4	.825
STS mortality score	6 (± 7)	6 (± 6)	.562
SYNTAX score	29.5 (± 13.7)	30.3 (± 13.2)	.595

IABP indicates intra-aortic balloon pump; NYHA, New York Heart Association; pVAD, percutaneous ventricular assist device; SD, standard deviation; STS, Society of Thoracic Surgeons; SYNTAX, Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

Methods

Study Design and Participants

The PROTECT II study design and methods have been published previously.[14] In brief, PROTECT II was conducted in 112 sites in the United States, Canada, and Europe. Each site had to demonstrate previous experience with hemodynamic support for nonemergent high-risk PCI. A predetermined need for hemodynamic support, which was assessed by the treating physician, was required to qualify the patient for enrollment. Between 2008 and 2010, 216 patients who met the eligibility requirements received a pVAD and 211 received an IABP and were enrolled at US hospitals, with 38 of these facilities agreeing to participate in this economic study.

All patients (mean age, 68 years) had a history of heart disease; 81% of them were men.

The study population was very well matched in terms of demographics, previous cardiac history, and degree of heart failure as described in **Table 1**, which shows no statistical differences among these and other baseline attributes. The study was approved by the institutional review board at each participating institution.

Analytic Approach

The results of the PROTECT II clinical trial were analyzed for clinical and economic benefits. Major adverse events (AEs), including death, myocardial infarction, stroke, repeat revascularization, need for cardiac or vascular operations (including vascular operations for limb ischemia), acute renal dysfunction, aortic insufficiency, cardiopulmonary resuscitation or ventricular tachycardia requiring cardioversion, severe hypotension and angiographic failure,[14] and, more specifically, major adverse cardiovascular and cerebrovascular events (MACCEs), were tracked from the index procedure through 90 days of follow-up and compiled for both study arms to generate clinical comparisons.

MACCEs included large acute myocardial infarctions (AMIs),[17] major strokes, repeat revascularizations, and death. (AMI was defined as the development of new Q-waves or CK-MB elevation 8 times above the upper normal value within 72 hours after a PCI for periprocedural AMI, or more than twice the upper normal value beyond 72 hours of the PCI for spontaneous AMI.) When CK-MB was not available, troponin values were used instead using the same threshold. In addition, hospital charges, costs, and length of stay were measured for the 90-day episode of care (EOC), including the index admission and any related readmissions.

To predict the economic value of the hemodynamic support strategies under review beyond the period for which empirical data were collected, a Markov model (described below) was developed to estimate an incremental cost-effectiveness ratio (ICER) adjusted for approximation of patient perceptions of the quality of their gains in life expectancy. This metric is offered in recognition of the recent trend toward longer retention of members by health plans. Historically, member retention was 2 to 3 years on average[18]; however, increased

switching costs, uncertainty surrounding the impact of the Affordable Care Act, and payer consolidation have resulted in fewer choices for employers, leading to stabilization and extension of member retention patterns.[19,20]

Measures of Clinical Benefits

The index and 90-day postindex major AEs and MACCEs were assessed as clinical end points during the PROTECT II clinical trial, with the MACCE incidence rates forming the basis for the economic study, both for the 90-day EOC assessment and the 10-year model. It is important to note that all readmissions within 90 days were also assessed from a timing, diagnostic, and resource consumption standpoint. In addition, changes in the New York Heart Association (NYHA) functional classification during the study period were tracked to assess the pVADs' impact on quality of life.

Measures of Economic Benefits

A retrospective economic analysis of the PROTECT II trial was undertaken to measure hospital resource utilization and the costs incurred during the 90-day EOC. Hospital charges, costs, and length of stay were tracked for medical or surgical and critical care levels of service during the index admission, as well as for hospital readmissions, including repeated revascularization procedures. Primary data sources for index admissions and readmissions were the clinical case report forms and copies of detailed hospital bills, as well as Centers for Medicare & Medicaid Services UB04 forms. Although these forms provided billed charges, such charges were converted to cost via institution-specific cost-to-charge ratios using (1) total and (2) department-level billing data to enhance accuracy.

Index admission hospital bills were obtained for 133 (63%) patients with an IABP and 130 (60%) patients with a pVAD, and they were determined to be representative of the full clinical trial population. Charges and costs for patients receiving an IABP who were missing bills were estimated by selecting similar patients treated at the same group of hospitals from the Medicare Provider Analysis and Review file for the 2009 federal fiscal year. The charges and costs of index admissions for missing pVAD bills were modeled by extrapolating from the available billing records using a bootstrapping technique. Hospital bills were collected for approximately 36% of all-cause readmissions, and basic diagnostic and length-of-stay data were collected on all readmissions via the clinical case report forms.

For patients with missing bills, the charges and costs were imputed from the mean values for each study group. Hospital resource use and costs for the complete EOC were calculated as the sum of the index admissions and any subsequent readmissions irrespective of cause and/or primary diagnosis.

Structure and Specification of the Markov Model

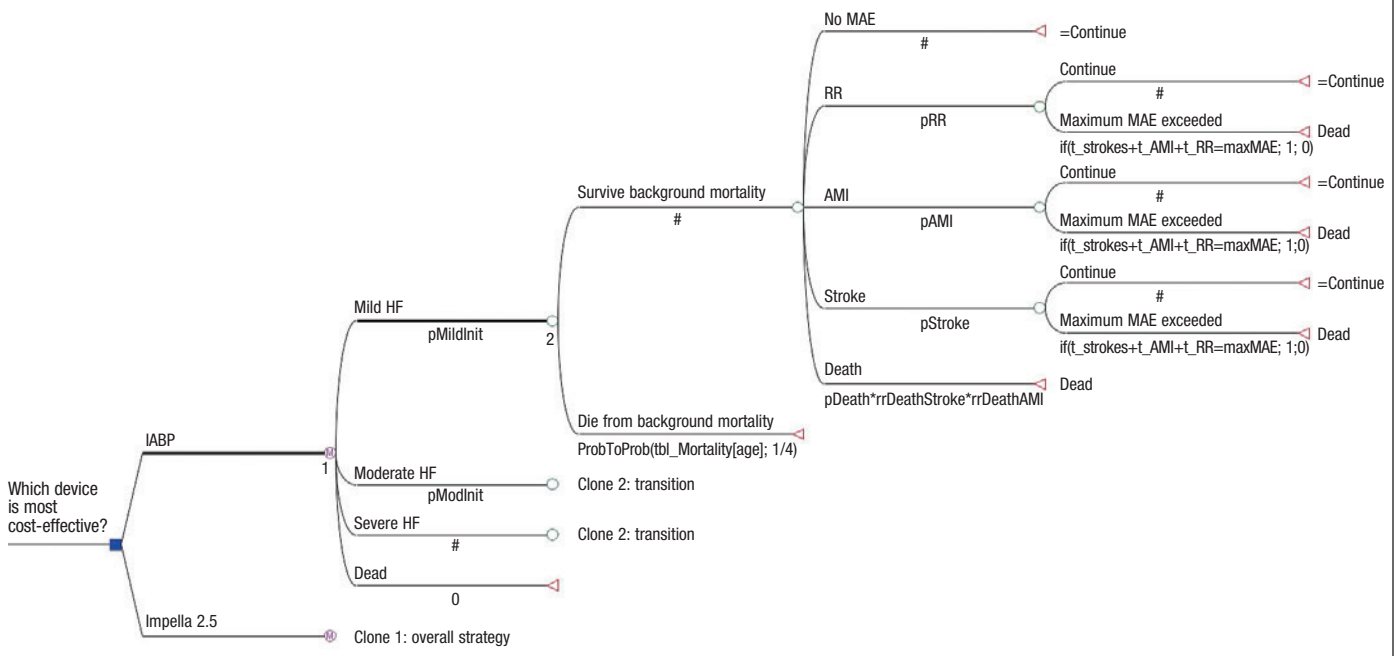
To further assess the value of pVADs in the treatment of patients undergoing high-risk PCIs, a Markov model was constructed using TreeAge 2011 Healthcare Pro (Williamstown, MA) to capture and to simulate the short- and long-term consequences of the lower rates of targeted MACCEs observed in the PROTECT II trial, as well as their impact on quality-adjusted life expectancy. A diagram of the decision tree is depicted in **Figure 2**. The specific measurements, assumptions, and sources underlying the input parameters used to generate the model outputs are detailed in the Appendices (available online at AHDBonline.com).

The EOC in the PROTECT II study and the last date of follow-up were 90 days after the procedure. Our model simulates the course of treatment of a hypothetical cohort based on the PROTECT II outcomes at 90 days. Our base-case simulation used a long-term, 10-year time horizon (40 cycles of 90 days each).

The application of the 90-day trial outcomes as the basis for the long-term, 10-year time frame analysis in our study conforms to accepted guidelines for cost-effectiveness analyses, as outlined by Weinstein and colleagues in the *Report of the ISPOR Task Force on Good Research Practices*.[21] They wrote, "Lifetime horizons are appropriate for many models and are almost always required for models in which options have different time-varying survival rates. Shorter horizons may be justified if survival and long-term chronic sequelae do not differ among options or based on an understanding of the disease process and the effect of interventions. In any case, the lack of long-term follow-up data should not be used as a rationale for failing to extend the time horizon as long as is relevant to the decision under analysis."[21]

On completion of the index procedure, the patients entered 1 of 4 "health states" reflecting the extent of heart failure (mild, moderate, or severe), scored by their NYHA functional classification or cardiac or cerebrovascular death. Subsequent Markov nodes simulated postprocedural MACCEs, including large AMI, major stroke, repeat revascularization and cardiac-related mortality, as well as cost consequences over the model's 10-year time horizon. It should be noted that these are not mutually exclusive transitional events; a stroke or repeated revascularization could take place after an AMI, and the model permits any combination of MACCEs to occur after the index event. Clinical and cost parameters during the initial 90-day EOC—spanning from the initial high-risk PCI admission, during which a pVAD or IABP was inserted (index admission) through the 90-day

Figure 2 Structure of the Markov Model



AMI indicates acute myocardial infarction; IABP, intra-aortic balloon pump; HF, heart failure; MAE, major adverse event; pAMI, probability of an AMI; pRR, probability of repeated revascularization.

follow-up period—were based on empirical findings from the PROTECT II trial and associated claims data.

Device costs in the model were set at $20,000 for the pVAD and $1000 for the IABP. Capital costs common with the pVAD and the IABP were excluded from the analysis. Future probabilities of MACCEs (a defined subset of the PROTECT II composite of major AE end points), quality-of-life utility adjustments, and accrual of costs were assigned according to estimates derived from the published literature. Costs and utilities were discounted at 3%.

Our analysis was limited to the direct costs of inpatient medical care, which account for 65% of IABP total costs and 70% of pVAD costs, and are the primary driver of resource consumption for the clinical condition under investigation.[22] This study, therefore, adopted the perspective of the healthcare system rather than the perspective of economic consequences to society at large.

Model Assumptions (Post–90-Day Cycles)

Cost parameters. A cost was estimated for nonfatal MACCE-associated treatment during the first and subsequent years based on analysis of site billing data and literature review. Long-term costs were assigned to AMI, stroke, and death. Repeat revascularizations were assumed to have incremental acute costs but no long-term and ongoing costs. A cost for death was assigned only if the death was associated with the patient reaching the maximum number of nonfatal MACCEs for their health state as determined by the expert opinion of independent specialists in interventional cardiology and cardiothoracic surgery. Deaths attributable to the natural course of heart failure and/or other-cause mortality were assumed to not have a resource-intensive, high-cost period immediately preceding death.

Clinical parameters. The Markov model was constructed for patients to experience 1 of the following 5 clinical consequences in each 90-day cycle:

- No MACCE (resulting in no disutility, no increased costs or no increased risk of death)
- AMI (resulting in a permanent disutility, increased costs, and an increased risk of death)
- Stroke (resulting in a permanent disutility, increased costs, and an increased risk of death)
- Repeat revascularization (resulting in a temporary disutility, a one-time incremental cost, and no increased risk of death)
- Cardiac or cerebrovascular death (resulting in a final utility weight of zero and a one-time incremental cost of death).

For these post–90-day cycles, the nonfatal MACCE probabilities were estimated by tapering (using cycle tiers)

and then leveling the incidence rates observed in the PROTECT II study at a pace that generated 10-year incidence rates generally consistent with the literature. To be conservative, probabilities for all nonfatal MACCEs were held constant after year 5 to reflect no differential between the study groups.

Survival parameters. The Seattle Heart Failure Model and several longitudinal cardiac mortality studies were the primary sources used to project survival based on NYHA functional classification as recorded at study entrance.[23-26]

Health utility parameters. Because the original study design did not provide for the development of an instrument to directly measure QALYs specific to the context and patient population of the trial, all patients were assigned a baseline utility weight according to their NYHA functional classification at study onset as derived from the Tufts Medical Center's Cost-Effectiveness Analysis Registry.[27] For patients who experienced a nonfatal MACCE, a "disutility" value was applied that discounted the quality of life subsequent to the occurrence of the particular event. Disutility weights were based on QALY values included in the Tufts registry and reported in the literature for the MACCEs of interest.[28-38] An incremental cost per QALY was calculated as follows:

$$\text{ICER} = \frac{(\text{Mean costs pVAD}) - (\text{mean costs IABP})}{(\text{Mean QALYs pVAD}) - (\text{mean QALYs IABP})}$$

Results

Clinical Benefits

Key clinical findings from the PROTECT II trial are presented in **Table 2**, along with levels of significance associated with differences between study groups. Major AE rates at 90 days for the pVAD were 40.0% versus 51.0% for an IABP (P = .023), a 22% relative reduction, including a 52% relative reduction in repeat revascularization (6.0% for a pVAD vs 12.4% for an IABP; P = .024). A significant portion of the differential in AE rates was observed after hospital discharge, with a 56% relative reduction in major AE rates (P = .002). More specific, overall MACCE rates for the study period were significantly reduced by 29% (P = .033). Finally, the advantage in major AE and MACCE reduction evidenced by the pVAD increased as the trial progressed over the 90-day period, a trend worth noting for extended model projections.

Economic Benefits

Comparative results for the economic variables under review during the 90-day time period of the PROTECT II trial are presented in **Table 3**. Hemodynamic support with a pVAD demonstrated reductions in overall length of stay, with mean hospital days for the entire EOC of 9.6 days for the pVAD and 10.7 days for an IABP (P = .026), a 10% relative reduction. Moreover, the median reduction in EOC length of stay was 2 days (7 days vs 9 days, respectively, or a 22% reduction; P = .008). The primary driver of this reduction was a 2-day length-of-stay savings during readmissions for patients with a pVAD, or a 29% relative reduction (P <.001). In addition, patients with a pVAD experienced a 40% relative reduction in critical care length of stay during readmissions (3.88 days with a pVAD vs 7.00 days with an IABP; P = .145).

Table 2 Key Clinical Findings from the PROTECT II Trial

Adverse event	IABP (N = 211), %	pVAD (N = 216), %	*P* value
Repeat revascularization	12.4	6.0	.024
Major AE rate	51.0	40.0	.023
Major AE rate after hospital discharge	18.1	7.9	.002
MACCE	31.0	21.9	.033

AE indicates adverse event; IABP, intra-aortic balloon pump; MACCE, major adverse cardiac and cerebrovascular event; pVAD, percutaneous ventricular assist device.

With regard to charge data, the mean charge for the index stay was lower for an IABP than for the pVAD ($124,778 vs $154,470, respectively; P <.001). By contrast, readmission charges were substantially lower for the pVAD than an IABP ($35,855 vs $102,260, respectively; P <.001), resulting in comparable 90-day EOC charge levels ($172,564 for a pVAD and $172,758 for an IABP; P = .785) despite the inclusion of the higher pVAD acquisition charge.

Given the variation in charge levels and accounting across facilities, we also calculated hospital cost levels using facility-specific cost-to-charge ratios to generate more stable economic results (Table 3). The mean cost of the index admission was higher for patients with a pVAD than for patients with an IABP ($47,667 vs $33,684, respectively; P <.001) largely as a result of the device acquisition cost. However, this upfront incremental cost for a pVAD was offset by its lower mean readmission costs than for the IABP ($11,007 vs $21,834, respectively; P <.001).

Lower mean readmission costs for the pVAD were attributable in part to the previously noted 40% reduction in critical care unit length of stay (ie, 3.12 fewer days on average) in patients with the pVAD for which hospital bills were secured. Of note, the projected payer cost for these readmissions was substantially similar to the reported hospital costs based on estimated diagno-

Table 3 Mean Values for Economic Measures from the PROTECT II Trial

Economic variables	Treatment			
Index admissions, all cases	**IABP (N = 211)**	**pVAD (N = 216)**	**Difference**	***P* value[a]**
Total charge	$124,778	$154,470	$29,692	<.001
Total cost	$33,684	$47,667	$13,983	<.001
LOS, days	7.4	7.1	–0.30	.331
Readmissions, all cases[b]	**IABP (N = 100)**	**pVAD (N = 108)**	**Difference**	
Total charge	$102,261	$35,856	–$66,405	<.001
Total cost	$21,834	$11,007	–$10,827	<.001
LOS, days	7.0	5.0	–2.0	<.001
EOC, all cases[c]	**IABP (N = 211)**	**pVAD (N = 216)**	**Difference**	
Total charge	$172,758	$172,564	–$194	.785
Total cost	$44,032	$53,171	$9139	<.001
LOS, days[d]	10.7	9.6	–1.10	.026

[a]*P* values derived from the nonparametric Mann-Whitney test. Statistical significance is reached when *P* <.050.
[b]Readmission sample size (N) represents the total number of readmissions, not the total number of study subjects that experienced at least 1 readmission.
[c]The pVAD case cost reflects costs derived for actual billed charges. For the incremental cost-effectiveness ratio model, pVAD's index and EOC costs were increased by approximately $5000 to align the study data with the actual hospital acquisition cost for the pVAD as reported by the manufacturer.
[d]The median values for EOC LOS are 9 days for IABP and 7 days for pVAD (*P* = .008).
EOC indicates episode of care; IABP, intra-aortic balloon pump; LOS, length of stay; pVAD, percutaneous ventricular assist device.

Table 4 Base-Case Results for the Markov Model (10-Year Time Horizon)

Estimated outcomes	IABP (N = 211)	pVAD (N = 216)
Cost		
Mean, $	75,655.58	85,896.66
Minimum, $	71,906.62	2090.03
Maximum, $	80,032.57	9382.27
Standard deviation, $	1467.07	1285.73
Effectiveness, QALYs		
Mean	2.22	2.48
Minimum	2.11	2.36
Maximum	2.34	2.59
Standard deviation	0.04	0.04
Cost-effectiveness		
Incremental cost, $		10,241.08
Incremental QALY		0.26
Estimated ICER, $		39,388.77

IABP indicates intra-aortic balloon pump; ICER, incremental cost-effectiveness ratio; pVAD, percutaneous ventricular assist device; QALY, quality-adjusted life-year.

sis-related group assignments, subject to negotiated rate differences that a particular plan may experience. The overall EOC costs averaged $53,171 for patients with the pVAD and $44,032 (*P* <.001) for patients with an IABP, a $9139 difference.

Cost-Effectiveness Analysis

Although the 90-day data are helpful for payer decision makers, a 10-year Markov simulation using the 90-day base-case parameters as an anchor for the model was used to project relative value over a longer time horizon. The estimated 10-year incremental cost for a pVAD relative to an IABP was $10,241, with an estimated incremental gain of 0.26 QALYs (**Table 4**). This equates to an ICER of $39,389 per QALY, which is below the widely accepted willingness-to-pay thresholds of $50,000 and $100,000 for other advanced cardiovascular technologies.[39-44]

Sensitivity Analyses

The base-case results do not take into consideration the uncertainty inherent in point estimates assumed for base-case parameters. A Monte Carlo analysis with second-order probabilistic sensitivity analysis (2-dimensional probabilistic sensitivity analysis) was conducted applying gamma and triangular distributions, respectively, to the EOC cost (1 standard deviation) and mortality (±10%)

variables. **Figure 3** shows the results of the 2-dimensional probabilistic sensitivity analysis to illustrate the robustness of the model to simultaneous variation of these input parameters randomly drawn from their respective probability distributions for 1000 replications of the Markov simulation. The position of the points in the northeast quadrant indicates that there is a high probability that pVAD is more costly, but more effective, than IABP.

Further interpretation of the cost-effectiveness results is facilitated by the cost-effectiveness acceptability curves presented in **Figure 4**. The horizontal axis defines various levels of societal willingness to pay for an intervention that yields better outcomes at a higher cost. In the United States, a range of $50,000 to $100,000 per QALY is frequently cited as describing the upper range of "good value for the money."[39-44] The curves indicate the likelihood that a technology would be considered "cost-effective" over a broad range of willingness-to-pay thresholds.

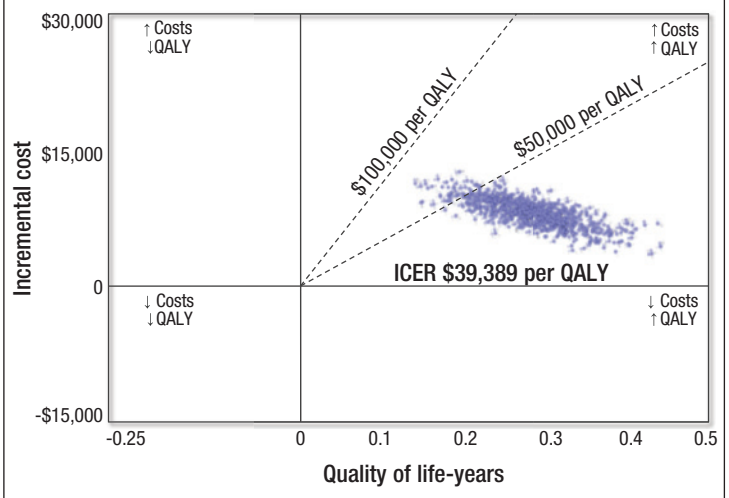
One-way sensitivity analyses (**Table 5**) were also performed to test the robustness of the model relative to key assumptions. The results revealed that the model was moderately sensitive to changes in the time horizon, death probabilities, EOC cost, MACCE probabilities, and the cost of death. The impact of the level of disutility associated with the MACCEs of AMI and stroke was minimal, given that these events occurred in a minority of the patients flowing through the model.

Discussion

Many of the newly introduced treatment regimens specifically target conditions that are common and costly, such as AMI and heart failure. As these interventions proliferate, decision makers will need to understand and balance the short-term costs of procedures versus the long-term costs for ongoing care with respect to improvement in objective clinical outcomes. In this context, medical technology will need to evolve in ways that offer outcome-based solutions that lead to increased quality and shared savings opportunities for all stakeholders.

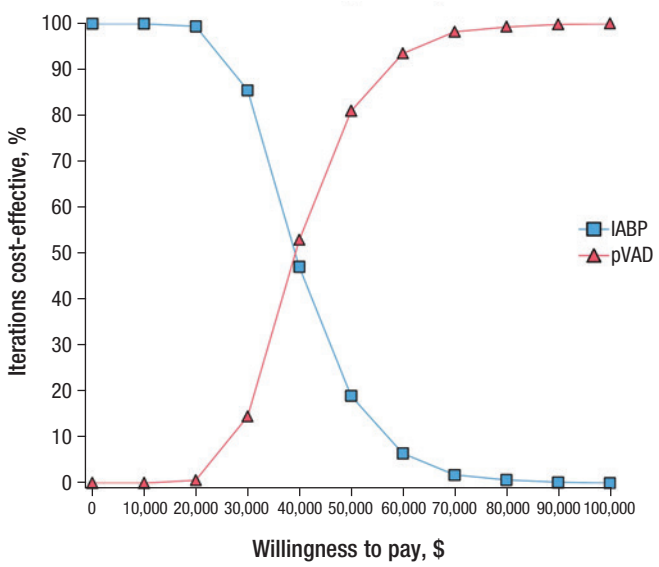
The introduction and increased adoption of pVADs challenges the traditional paradigms that are currently used to assess medical technology. In the case of pVAD utilization, the acquisition cost is significantly greater than standard-of-care devices and must be assessed in a context of potentially decreasing the frequency of serious major AEs and lowering the rates of readmission over a reasonable time horizon. At 90 days after a procedure, patients in the PROTECT II study receiving pVAD support experienced a 29% reduction in MACCE and a 2-day median decrease in hospital days relative to IABP, in part because of a reduction associated with fewer expensive critical care days.

Figure 3 Probabilistic Sensitivity Analysis Scatter Plot



ICER indicates incremental cost-effectiveness ratio; QALY, quality-adjusted life-year.

Figure 4 Cost-Effectiveness Acceptability Curves for pVAD versus IABP



IABP indicates intra-aortic balloon pump; pVAD, percutaneous ventricular assist device.

The PROTECT II clinical study demonstrated that the pVAD provided superior hemodynamic support during the index PCI compared with the IABP.[14] Fewer patients were discharged from the catheterization laboratory with the pVAD in place after a procedure compared with an IABP,[14] suggesting more hemodynamic stability in the pVAD group that may have also contributed to

Table 5 One-Way Sensitivity Analyses

Model parameter	Sensitivity range	ICER range, $ thousands
Episode of care costs[a]	Base case to +$5000	$39.5 to $58.5
Major AE taper[b]	Base case to year 2	$39.5 to $47.8
AMI disutilities	–0.24 to –0.12	$39.5 to $40.7
Stroke disutilities	–0.5 to –0.3	$39.5 to $41.8
Cost of death[c]	Base case to $0	$39.5 to $45.1
Death probabilities	0% to 10%	$39.5 to $59.3
Discount rate	0% to 5%	$33.5 to $43.1

[a]Base case, $58,194 for pVAD episode of care costs.
[b]Base case, nonfatal major adverse cardiovascular and cerebrovascular event probabilities equilibrate at year 5.
[c]Base case, $23,774 for cost of death.
AMI indicates acute myocardial infarction; ICER, incremental cost-effectiveness ratio; AE, adverse event; pVAD, percutaneous ventricular assist device.

the shorter length of stay. It is also hypothesized that the enhanced circulatory support provided by the pVAD during the index PCI allowed the investigators to use, more often and more aggressively, adjunctive therapies, such as rotational atherectomy on complex calcified lesions. This potentially led to a more complete revascularization and, consequently, to fewer readmissions for target and nontarget repeat revascularizations, less in-stent thrombosis, and less spontaneous myocardial infarction after discharge in these particular patients.

Similar to other studies that suggested the long-term effect of hemodynamic support on outcomes, the Kaplan Maier curves in the PROTECT II trial continued to diverge over time, with fewer overt major AEs requiring readmission in the pVAD arm, emphasizing the potential beneficial long-term effect of a more potent circulatory device in this high-risk patient population.

The clinical findings also indicate that AE rates were further reduced in the second half of the study, suggesting that an early learning curve with respect to the pVAD technology may be mitigated over a relatively short period of time. If true, this observation presents an opportunity for improved outcomes and increased efficiency based on appropriate patient selection and well-defined treatment protocols. It is important to note that the majority of the billing records for this economic analysis were obtained for patients enrolled during the first half of the study and early in the learning curve, suggesting that treatment costs and associated cost-effectiveness metrics are conservatively reported.

Furthermore, a recently published study of the budget impact of pVAD utilization on commercial payers demonstrated that the incremental costs of accelerated adoption are minimal based on a retrospective commercial claims analysis that identified a low incidence rate for this patient cohort in the commercial population.[22] Moreover, that study confirmed the results reported in our economic analysis that postindex costs are unremarkable when compared with the index costs of care.

The use of Markov modeling provides decision makers with another lens through which to view the extended relative benefits of a particular medical technology. Specifically, the 10-year ICER (equating to $39,389 per QALY) reported in this study reflects the long-term value of the device under study and is derived from a modest increase in quality of life for patients with a pVAD, supplemented by a modest extension of life expectancy that is driven by reduced MACCEs. It is also telling us that the acquisition cost of a pVAD begins to dissipate shortly after the initial 90 days (during which the device is purchased), and that inpatient costs begin to moderate annually based on fewer MACCEs experienced by patients treated with the new device.

The enactment of the Affordable Care Act will likely accelerate a fundamental transformation in the delivery of acute and chronic care that may ultimately lead to an increased use of value-based payment strategies. This legislation encourages the formation of accountable care organizations that integrate hospitals, physicians, and other care providers to improve the coordination of care and overall efficiency, with the prospect of shared savings as the reward.

As this transformation evolves, value-based outcome measures will be expanded to encompass extended EOC benefits, patient-reported outcomes, and quality-of-life measures.[45] Providers of cardiovascular care will be particularly affected, because they will have to carefully consider the costs and benefits of multiple alternative therapies for managing a population that is increasingly older, and with a growing prevalence of complex chronic conditions. Analyses similar to those presented in this article should help decision makers adjust to the rapidly changing landscape of healthcare delivery, insurance coverage, and reimbursement policies.

Limitations

The present study was performed from the perspective of the United States only, and the results may not be applicable to other healthcare systems.

Although index billing data were available for approximately 62% of the study population, modeling was necessary for the remainder of the patients, as well as for the longer time horizon.

Nonacute services (eg, professional, rehabilitation, and other ancillary care) were not included in this analysis and should be considered for future studies that examine incremental cost-effectiveness associated with the use of pVADs.

Measures of utility or health-state preference were not included in the original design of the PROTECT II trial. Accordingly, the QALY weightings used in this economic study were based on literature-derived utility scores. To remedy this shortcoming, future research efforts should endeavor to explicitly incorporate study-specific indicators of health-state utility as perceived by patients enrolled in clinical trials.

Conclusions

This PROTECT II economic analysis demonstrated that the nonemergent use of a pVAD during high-risk PCI resulted in significant reductions in the risk of MACCE (including repeat revascularizations requiring a readmission), readmission costs, and length of stay, despite moderately higher 90-day EOC costs. Moreover, when a multiyear extended timeline is considered for judging the value of pVAD use, our study suggests that the incremental expenditure per QALY gained is cost-effective and well within the willingness-to-pay range that is widely accepted for other advanced cardiovascular technologies. The short-term and the longer-term findings presented in this article have implications for medical coverage decisions and underscore a value proposition that health plans and accountable care organizations should carefully consider during the technology assessment process.

It is our hope that this study encourages researchers and health plans to consider developing new metrics that offer a more practical guidance with regard to judging new technology. Toward this end, it may be useful to construct a quality-adjusted per-member per-month metric that acknowledges the incremental per-member per-month cost of a technology for a defined period of time and adjusts it to account for measurable indicators of quality, such as increased patient satisfaction (ie, patient-reported outcomes), reduced short-term AEs, and/or better management of comorbidities. ■

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Author Disclosure Statement

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STAKEHOLDER PERSPECTIVE

Careful Selection of Candidates for Percutaneous Ventricular Assist Device Is Crucial

By Raymond L. Singer, MD, MMM, CPE
Chief, Division of Cardiothoracic Surgery, Vice Chair, Quality and Patient Safety, Department of Surgery, Lehigh Valley Health Network, Allentown, PA

PAYERS: Approximately 6 million people in the United States have heart failure (HF), and nearly 700,000 new cases are diagnosed annually. The incidence of HF approaches 10 per 1000 population after age 65 years. It is estimated that by 2030, an additional 3 million people will have HF, a 25% increase in prevalence.

The most common cause of HF in patients aged >65 years is advanced coronary artery disease (CAD). These compromised patients are likely to have comorbidities that may preclude them from being candidates for coronary artery bypass graft (CABG) surgery. As an alternative, the less-invasive but high-risk option of a percutaneous coronary intervention (PCI) can serve this population well, improving quality of life (QOL), reducing major adverse events (AEs), as well as reducing hospital admissions.

For patients with ventricular dysfunction and complex coronary anatomy, the use of an adjunct mechanical device for vascular support during high-risk PCI improves outcomes. The intra-aortic balloon pump (IABP) provides ischemic protection by increasing the diastolic pressure and improves cardiac output by providing after-load reduction. The Impella 2.5 is a percutaneous ventricular assist device (pVAD) that reduces the workload of the left ventricle. Although this device lacks the ischemic protection of an IABP, it is much more effective in reducing the left ventricle workload.

The PROTECT II study by Gregory and colleagues is a prospective, multicenter, randomized trial comparing the Impella 2.5 pVAD to the use of an IABP in patients who require high-risk PCI.

Historically, the IABP has been the most widely used mechanical support device for the failing left ventricle; however, it only modestly improves hemodynamic parameters. Therefore, the hypothesis of the PROTECT II trial is that the Impella 2.5 system is superior to the IABP in preventing intra- and postprocedural major AEs during high-risk PCI.

The Impella 2.5 arm of PROTECT II indeed had a 22% relative reduction in major AEs, as well as 56% fewer major AEs after hospital discharge. Repeat revascularizations were also lower by 52% at 90 days. Repeat revascularization impacts readmission rates and patient QOL. Costs were higher in the Impella 2.5 arm during

STAKEHOLDER PERSPECTIVE *Continued*

the hospital index stay; however, the results showed lower costs for the Impella 2.5 arm over the IABP arm during readmissions through 90 days.

From a payer perspective, this study provides strong evidence to support the use of Impella 2.5–assisted PCI in patients with ventricular dysfunction and complex coronary anatomy who require high-risk, mechanically assisted PCI. The use of this device significantly reduces major AEs, improves quality-adjusted life-years, and is cost-effective. Reductions in repeated revascularizations, readmission costs, and length of stay are particularly important in this era of healthcare reform, in which readmission rates will impact reimbursement. It is equally important to recognize that case selection is critical. The Impella 2.5 pVAD remains an expensive technology, and, like all invasive devices, its use is not without risk.

Furthermore, payers should be wary about overuse. Using this device in patients who would have had successful PCI outcomes without it is unproductive and wasteful of precious healthcare dollars. Therefore, the patient's clinical condition and coronary anatomy should clearly support the indication for a pVAD-assisted PCI.

Clinical judgment based on defined protocols and best practice observations are paramount. Like all new and expensive technologies, the appropriateness of case selection should be reviewed, and the annual use of each provider and/or institution should be monitored to ensure best practice standards.

PATIENTS: Patients with advanced CAD, impaired ventricular function, and congestive HF are faced with a poor QOL and compromised survival. Despite advances in medical therapy, myocardial revascularization remains the best option for this population of patients. But the pathway to achieve myocardial revascularization remains controversial. As a cardiovascular surgeon, I am particularly aware of the debates regarding best treatment options for patients with 3-vessel CAD and impaired ventricular function, particularly in patients with diabetes.

For example, the Bypass Angioplasty Revascularization Investigation trial concluded that CABG had better rates of survival than PCI in patients with diabetes.[1] More recently, the Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease trial reached a similar conclusion.[2] Even beyond diabetes, there are many trials that advocate surgical myocardial revascularization rather than PCI in patients with 3-vessel CAD and impaired ventricular function.

Therefore, the first issue facing this growing population of patients with advanced CAD, ventricular dysfunction, and HF is informed consent. As Dr Mark Hlatky stated recently, "Many PCIs today are ad hoc procedures, performed at the time of diagnostic coronary angiography, with the same physician making the diagnosis, recommending the treatment, and performing the procedure."[3] Therefore, it is important for patients to learn about all available treatment options, including medical therapy and CABG, along with a complete discussion of the benefits and risks of each treatment.

In the select population of patients who have failed medical therapy and who have been identified by an experienced cardiovascular surgeon not to be candidates for CABG, high-risk PCI using an adjunct mechanical device, such as an IABP or the Impella 2.5, is appropriate. The PROTECT II trial supports the conclusion that Impella 2.5–assisted PCI significantly reduces major AEs and is more cost-effective than IABP-assisted PCI. The reductions in repeated revascularizations, readmission costs, and length of stay all impact QOL and provide greater clinical benefit for this high-risk patient population. ■

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